LATE EFFECTS OF INHALED $^{253}Es(NO_3)_3$ IN THE RAT

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The lungs of rats exposed to $^{253}Es(NO_3)_3$ aerosols sustained the greatest cumulative radiation dose, approximately 6-fold higher than the skeletal dose. Malignant lung tumors (incidence 8.5, 27.6%) were observed after a mean cumulative lung dose of 26 and 400 rad, respectively. Higher lung doses were associated with severe life shortening that precluded the expression of delayed effects. Osteosarcomas of the skeleton (incidence 6.9%) were found after a mean cumulative skeletal dose of 68 rad. Earlier studies, which showed a high incidence of bone tumors and relatively fewer lung tumors after intratracheal instillation of $^{253}EsCl_3$, were not confirmed in this study with inhaled $^{253}Es(NO_3)_3$.

Einsteinium-253 is a transuranic element with physical half-life of 20.5 days and alpha decay energy of 6.6 MeV. The isotope is of interest for comparing the effects of radiation dose rate and dose distribution with more long-lived transuranics. Earlier studies, using intratracheal instillation, produced bone tumors as the major late-developing malignancy after ^{253}Es incorporation. The present study is a follow-up, using the more normal inhalation route.

Groups of 60 male Wistar rats, 60 days of age, were held for life-span study of long-term effects following a single, nose-only exposure to one of three graded dose levels of $^{253}Es(NO_3)_3$ aerosols. The initial lung burdens (ILB), expressed as the mean with standard deviation, were 30 $\pm$ 8, 520 $\pm$ 130 and 6200 $\pm$ 1800 nCi, respectively. Initial lung burdens were estimated by external counting techniques applied soon after exposure, since the short physical half-life of ^{253}Es precludes later determination of lung deposition, e.g. at necropsy. Weight gain appeared to be depressed only by the highest dose level (6200 nCi ILB), while life-shortening effects were observed with both the high and medium dose levels, i.e., 6200 and 520 nCi ILB. Rats with the lowest dose, 30 nCi ILB, exhibited weight gain and mortality similar to untreated controls.

Einsteinium-253 retention in tissues (Figure 3.15) was determined by sacrificing and analyzing rats at intervals after $^{253}Es(NO_3)_3$ inhalation. The values are the means of either 5 or 10 rats with the standard deviation indicated for the lungs and the skeleton. Retention in the lungs was described by two exponential functions with effective half-lives of 1 and 10 days accounting for 65% and 35% of the ILB, respectively. Clearance from the skeleton and the testes was assumed to occur at the rate of the physical half-life (20.5 days) since biological clearance was not evident. Retention in the liver, kidneys and tracheobronchial lymph nodes was approximated with a single exponential function as an estimate of the buildup and clearance phases seen in these tissues. These retention parameters were used to calculate the accumulated radiation dose estimates listed in Table 3.9. The lungs accumulated the largest radiation dose, followed by the skeleton, kidneys and liver. The dose distribution pattern is similar to that reported for other transuranic nitrates following inhalation exposure.

The major long-term effect of $^{253}Es(NO_3)_3$ inhalation was the induction of lung tumors, as expected, because of the consistently high radiation dose to pulmonary tissues. Since the earlier study with intratracheally instilled ^{253}Es produced a preponderance of bone tumors, it is of interest to compare the dose-response results from these two studies (Table 3.10). Even though the estimated radiation dose to the lungs was greater in the intratracheally instilled rats, the incidence of lung tumors after

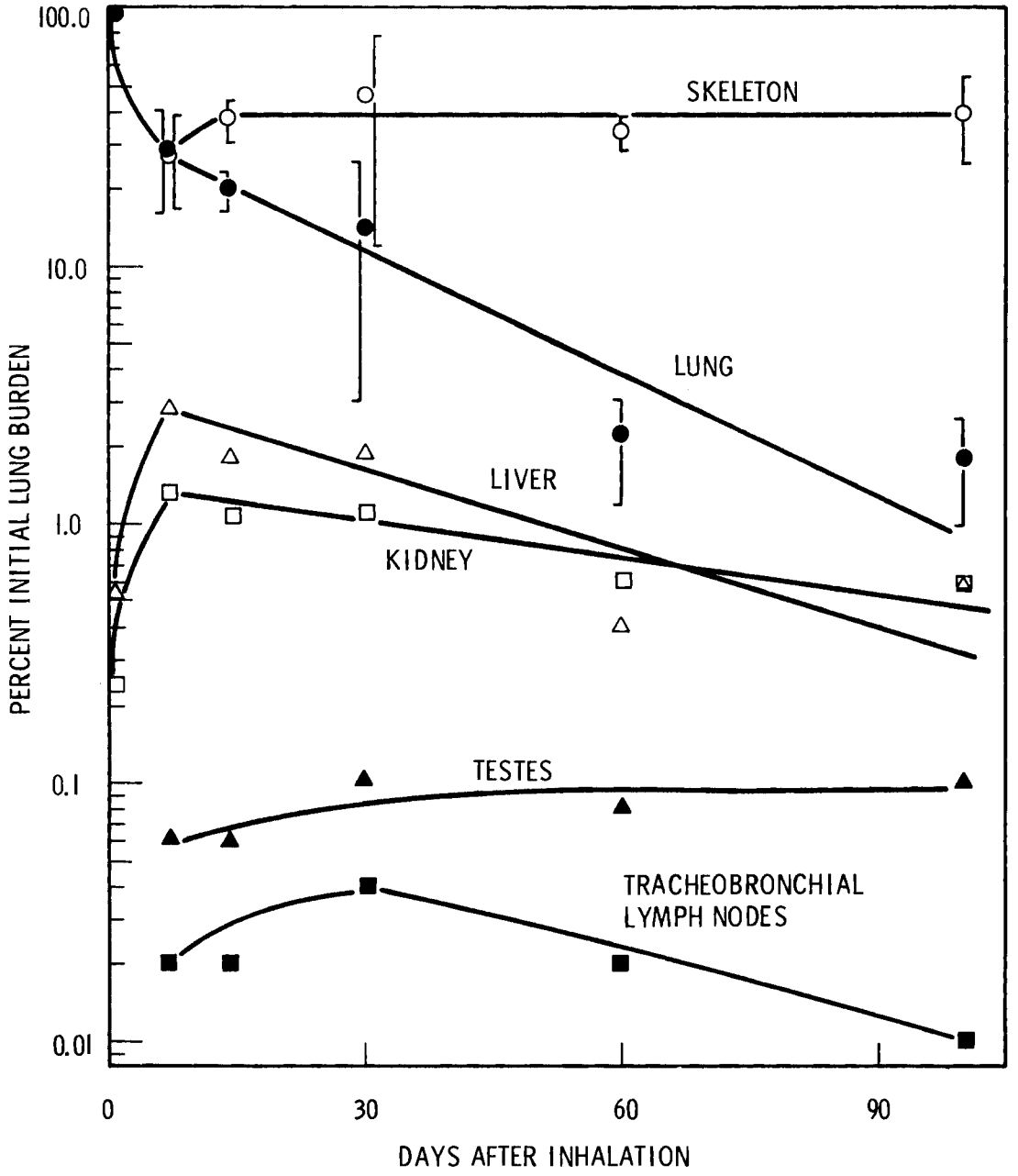

FIGURE 3.15. Distribution and Retention of Inhaled $^{253}Es(NO_3)_3$. (Values are corrected for radioactive decay; curves represent biological turnover.)

TABLE 3.9. Accumulated Radiation Dose in Tissues with Major ^{253}Es Deposition.

Mean Initial Lung Burden, nCi ± SD	Number of Rats	Cumulated Radiation Dose, rad					
		Lung	Liver	Skeleton	Testes	Kidney	Tracheo-bronchial Lymph Nodes
30 ± 8	60	24	0.28	4.2	0.06	1.1	0.17
520 ± 130	60	390	4.5	68	1	18	2.8
6200 ± 1800	60	4800	30	670	10	190	31

TABLE 3.10. Incidence of Lung Tumors Following Intratracheal Instillation (IT) of $^{253}EsCl_3$ Solutions and Inhalation (INH) of $^{253}Es(NO_3)_3$ Aerosols.

Mean Cumulative Lung Dose, rad[a]		Number of Rats		Avg. Survival Time, days		Rats with Lung Tumors		Lung Tumor Incidence, %	
INH	IT	INH	IT	INH	IT	INH	IT	INH	IT
8.1	—	3	—	705	—	0	—	0	—
26	38	59	48	710	707	5	2	8.5	4.2
400	1900	58	48	567	475	16	6	27.6	12.5
4800	9800	60	29	45	181	0	0	0	0
Control[b]		238		714		0	0	0	0

[a] Animals exposed by inhalation (INH) are from the present study. Animals exposed by intratracheal instillation (IT) are described in PNL Annual Report for 1974.
[b] Includes treated and nontreated controls from present study and 0.27 N HNO_3-exposed controls described in PNL Annual Report for 1975.

inhalation was higher. We believe this is a reasonable finding because the inhaled ^{253}Es is more uniformly distributed in the lung and irradiates more sensitive tissue than a comparable instilled dose. The differences in bone tumor incidence were more dramatic (Table 3.11), primarily because rats exposed by the intratracheal route accumulated large radiation doses to the skeleton and lived sufficiently long to express bone tumors. Following inhalation exposure, those rats with a high skeletal dose also sustained severe lung damage, resulting in early death due to radiation pneumonitis. The greater acute toxicity of inhaled ^{253}Es is attributed to its more uniform distribution throughout the lungs, resulting in total lung impairment, compared to a more localized, lobular deposition and damage following instillation. We conclude from these results that the long-term effects of inhaled ^{253}Es are similar to those observed after comparable radiation by other transuranic elements. The relatively short duration of intense alpha radiation characteristic of ^{253}Es appears to induce lung tumors at least as efficiently as a more protracted radiation insult. Bone tumors are expected to be more efficiently produced by ^{253}Es because a greater proportion of the short-lived radionuclide decays on sensitive bone surfaces.

TABLE 3.11. Incidence of Bone Tumors Following Intratracheal Instillation (IT) with $^{253}EsCl_3$ Solutions and Inhalation (INH) of $^{253}Es(NO_3)_3$ Aerosols.

Mean Cumulative Skeletal Dose, rad[a]		Number of Rats		Avg. Survival Time, days		Rats with Bone Tumors		Bone Tumor Incidence, %	
INH	IT	INH	IT	INH	IT	INH	IT	INH	IT
4	5	61	48	706	707	0	0	0	0
68	230	58	48	574	475	4	20	6.9	42
640	—	59	—	51	—	0	—	0	—
1100	1200	2	29	67	181	0	1	0	3.4
Control[b]		238		714		5[c]		2.1	

[a] Animals exposed by inhalation (INH) are from the present study. Animals exposed by intratracheal instillation (IT) are described in PNL Annual Report for 1974.
[b] Values represent combined controls from the present study and 0.27 N HNO_3-exposed controls reported in PNL Annual Report for 1975.
[c] Bone tumors were observed only in 5 of 97 treated control rats exposed to the aerosol vehicle (0.27 N HNO_3) used in the present study.